

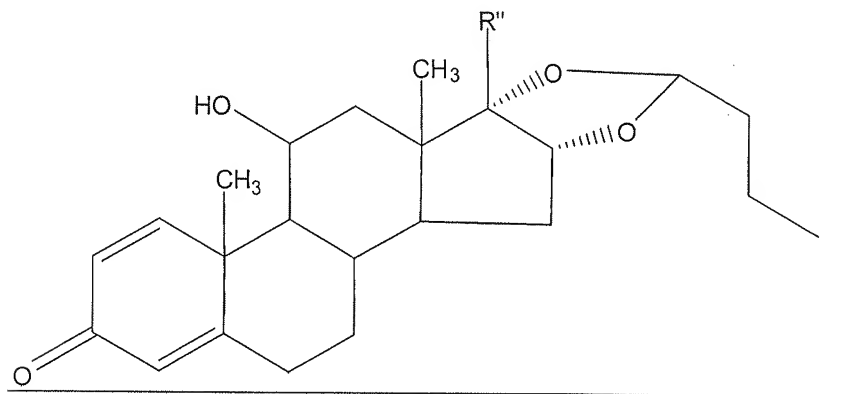
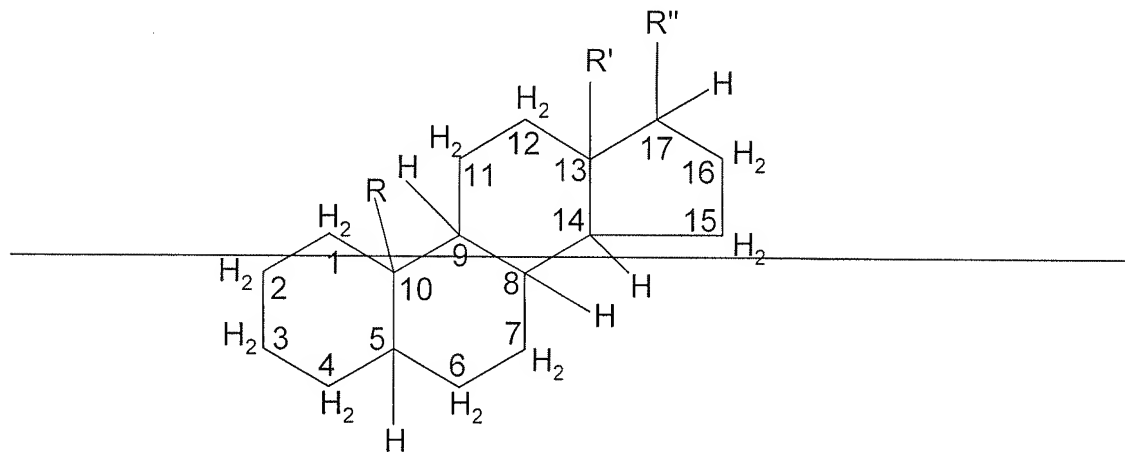
I. AMENDMENTS TO THE CLAIMS

Claim 1. (Currently Amended) Nitrooxy derivatives of steroidal compounds of general formula



or esters or salts thereof, wherein:

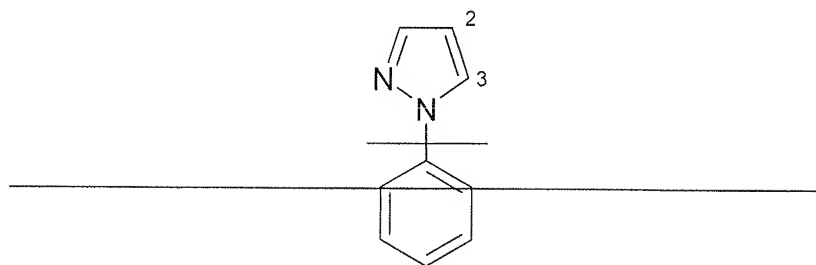
B is a steroidal radical having the following structure:



(IA)

wherein at the place of the hydrogen of the CH group, or of the two hydrogens of the CH₂-group indicated in the general formula, there can be the following substituents:

- in position 1-2: a double bond;
- in position 2-3 the following substituent:



_____ (IA-1);

_____ in position 2: Cl, Br;

_____ in position 3: oxo, O-CH₂-CH₂-Cl, OH, OCH₃;

_____ in position 4-5: a double bond;

_____ in position 5-6: a double bond;

_____ in position 6: Cl, F, Br, CH₃, CHO;

_____ the ring defined by the carbon atoms numbered 1, 2, 3, 4, 5, and 10 is an aromatic ring when B is the residue of an estrogen;

_____ in position 7: Cl, OH;

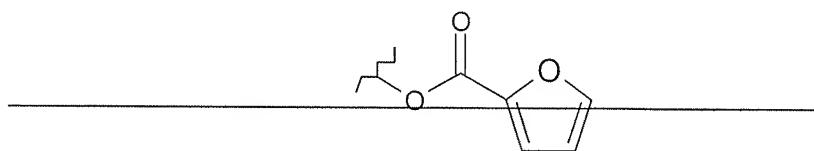
_____ in position 9: Cl, F, Br;

_____ in position 11: OH, oxo, Cl;

_____ in position 16: CH₃, OH, =CH₂;

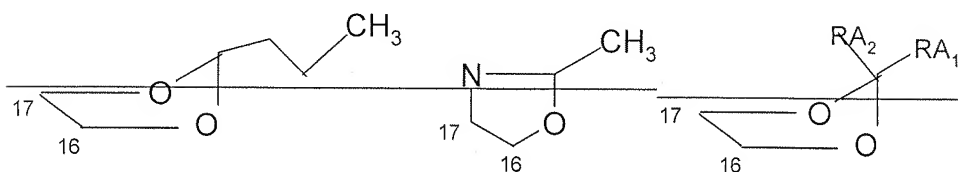
_____ in position 17: OH, CH₃, OCO(O)_{ua}(CH₂)_{va}CH₃ wherein ua is an integer equal to 0 or 1, va is an integer from 0 to 4, ethynyl (C≡CH);

or



(IA-2)

_____ in position 16-17 the following groups group:



_____(IA-3)_____ (IA-4)_____ (IA-5)

_____ wherein RA_1 is H, CH_3 ; RA_2 is C_4 - C_{40} linear or branched alkyl chain, preferably C_4 - C_3 , still more preferably CH_3 , or a saturated cycloaliphatic ring having 5-6 carbon atoms or an aromatic ring optionally substituted in para position with $N(R_{16})_2$ wherein R_{16} is a C_4 - C_{40} , preferably C_4 - C_4 , linear or branched alkyl; R and R' , equal to or different from each other, can be hydrogen or C_4 - C_4 linear or branched alkyls, preferably $R = R' = CH_3$ or $R = R' = H$;

_____ preferably B is a corticosteroid residue;

R'' in position 17 is $-(CO-L)-$, and a bivalent radical having one of the following meanings:

IB) $-(CO-L)_t-(X_O)_{t1}$, wherein $t = 1$ and $t1$ is 0 or 1, preferably 0;

IC) $L(X_O)_{t1}$, wherein $t1$ is 0 or 1, preferably 1;

the bivalent linking group L has the following meaning:

$-(CR_4R_5)-(O)-(CO)-$,

wherein $R_4 = R_5 = H$;

$(CR_4R_5)_{na}(O)_{nb}(CR_4'R_5')_{n'a}(CO)_{n'b}(O)_{n''b}(CO)_{n'''b}(CR_4''R_5'')_{n''a}$

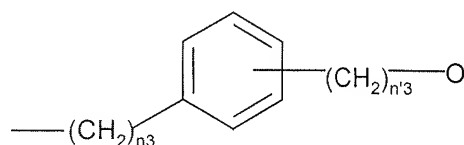
_____ wherein na , $n'a$, and $n''a$, equal to or different from each other, are integers from 0 to 6, preferably 1-3; nb , $n'b$, $n''b$ and $n'''b$, equal to or different from each other, are integers equal to 0 or 1; R_4 , R_5 , R_4' , R_5' , R_4'' , R_5'' , equal to or different from each other, are selected from H, C_4 - C_5 , preferably C_4 - C_3 , linear or branched alkyl;

_____ $X_O = O$, NH , NR_{16} wherein R_{16} is as above defined;

_____ the bond between the steroid and the linking group X_1 is of ester or amidic type;

X_1 is a bivalent linking group selected from the following group consisting of:

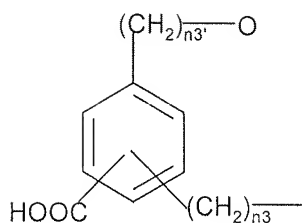
- Y_{AR1} :



(V)

wherein $n3$ is an integer from 0 to 5 and $[[n3]]$ $n'3$ is an integer from 1 to 3;

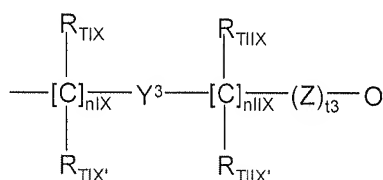
- Y_{AR2} :



(VI)

wherein n_3 is as defined above, and $n_{3'}$ is an integer from 1 to 3; and have the above meaning.

- Y_p :



(III)

wherein:

n_{IX} is an integer from 0 to 10, preferably 1-3;

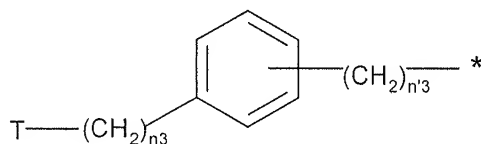
n_{IIX} is an integer from 1 to 10, preferably 1-5;

R_{TIX} , $R_{TIX'}$, R_{TIIX} , $R_{TIIX'}$, equal to or different from each other, are H or C_1 - C_4 linear or branched alkyl; preferably R_{TIX} , $R_{TIX'}$, R_{TIIX} , $R_{TIIX'}$ are H;

Y^3 is a saturated, unsaturated or aromatic heterocyclic ring, having 5 or 6 atoms, containing from one to three heteroatoms, preferably from one to two, said heteroatoms being equal or different and selected from nitrogen, oxygen, sulphur, preferably nitrogen;

t_3 is zero or 1;

Z has the following meaning:



(VI)

wherein:

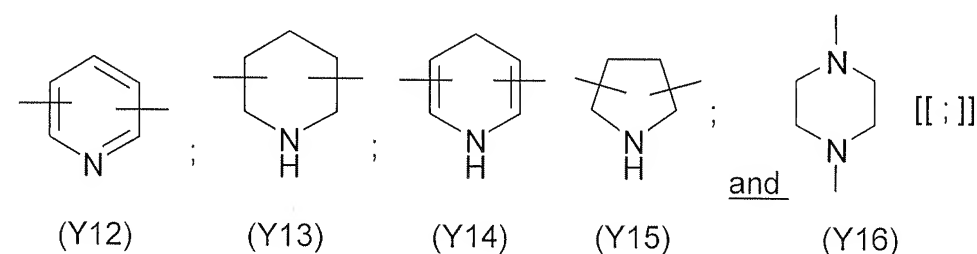
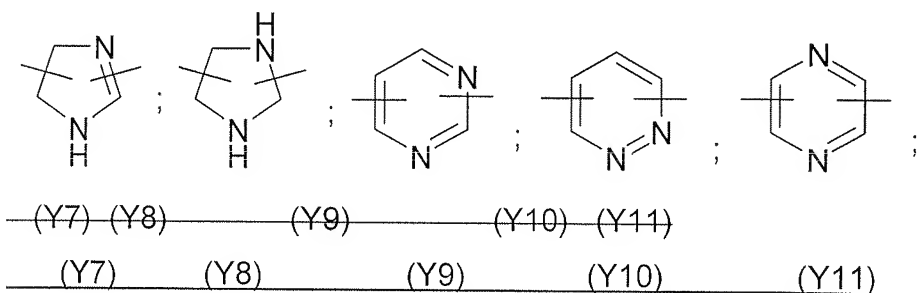
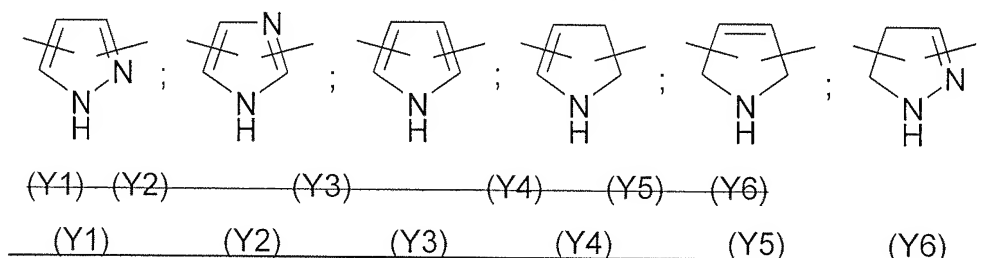
* shows the position of the ONO_2 group;

T has the following meanings is selected from the group consisting of: [:-]
 $-\text{COX}_3-[[,]]$ and $-\text{X}_3\text{CO}-$, wherein $\text{X}_3 = \text{S}, \text{O}, -\text{NH},$ or $-\text{NR}_{1\text{C}}$, wherein $\text{R}_{1\text{C}}$ is a $\text{C}_1\text{-C}_{10}$ linear
 or branched alkyl or $-\text{X}_6$ -as above defined;

~~$-\text{X}_3$ -as above defined;~~

and n_3 and n'_3 are as above defined.

Claim 2. (Currently Amended) Compounds according to claim 1, wherein Y^3 is
 selected from the following bivalent radicals:

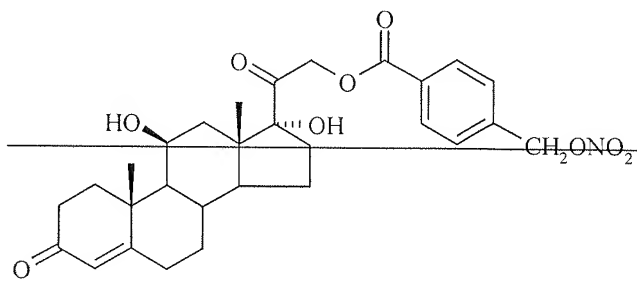


Claim 3. (Currently Amended) Compounds according to claim 2, wherein Y^3 is
 selected from the following group consisting of: (Y12), having the two free valences in
 the ortho positions with respect to the nitrogen atom; (Y16) with the two valences linked
 to the two heteroatoms[[:]]; and (Y1) (pyrazol) 3,5-disubstituted; ~~(Y16) is particularly~~
 preferred.

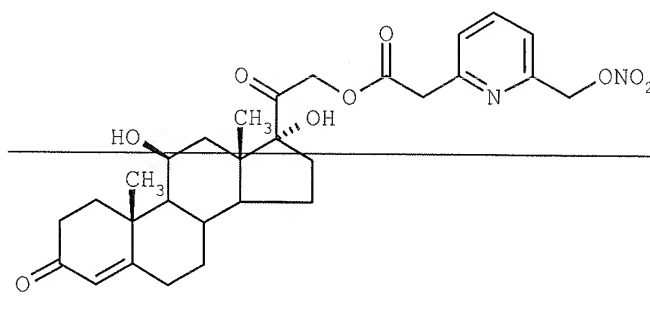
Claims 4-7. (Canceled)

Claim 8. (Currently Amended) Compounds according to claim 1 any one of
claims 1-3, selected from the following group consisting of:

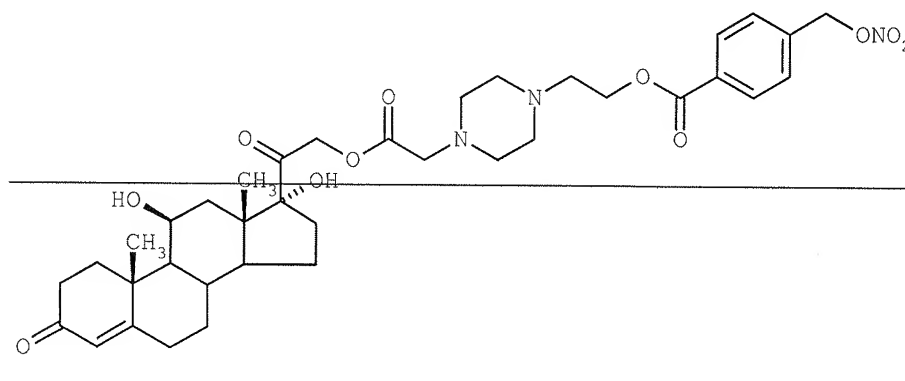
~~Hydrocortisone-21-(4'-nitrooxymethyl) benzoate~~



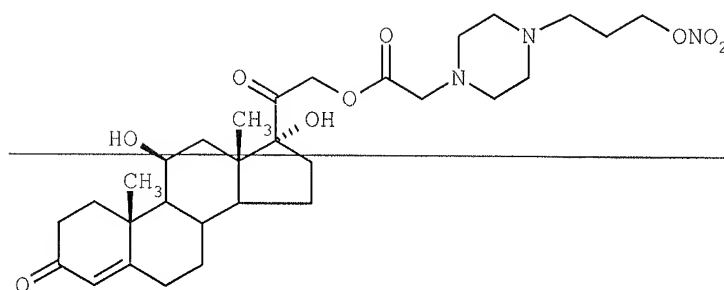
~~Hydrocortisone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]-acetate]~~



~~Hydrocortisone-21[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy]-ethyl]-1-piperazinyl]acetate]~~

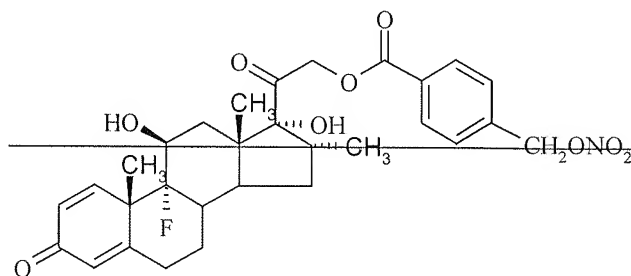


~~Hydrocortisone-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl]-acetate]~~



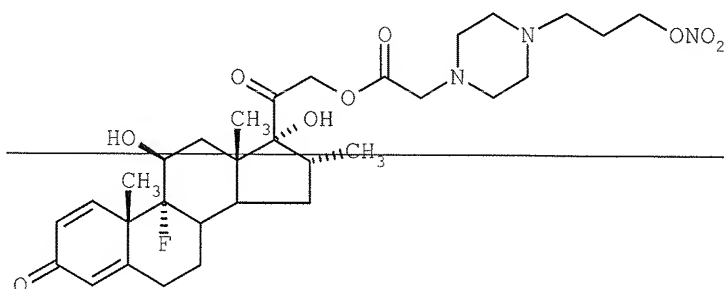
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Dexamethasone 21-(4'-nitrooxymethyl)benzoate



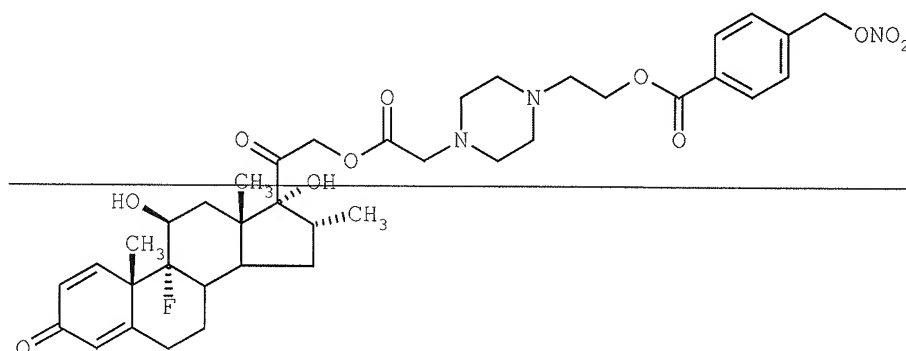
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Dexamethasone 21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl]acetate]



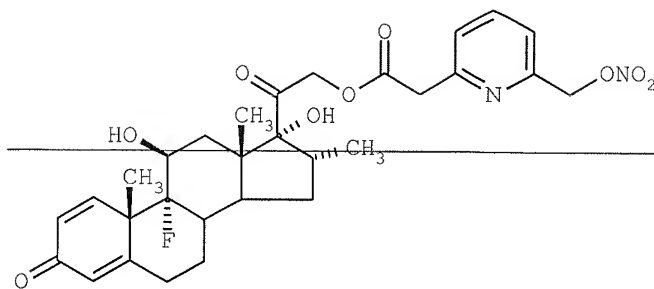
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Dexamethasone 21-[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy]ethyl]-1-piperazinyl]acetate]



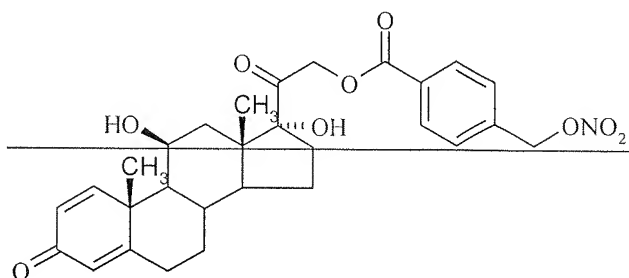
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Dexamethasone 21-[2-[6-(nitrooxymethyl)-2-pyridinyl]acetate]



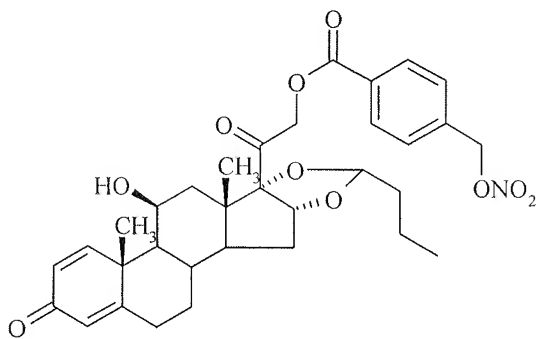
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Prednisolone 21-(4'-nitrooxymethyl)benzoate



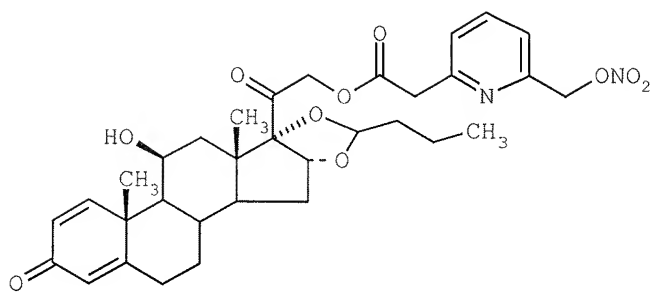
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Budesonide 21-(4'-nitrooxymethyl)benzoate:



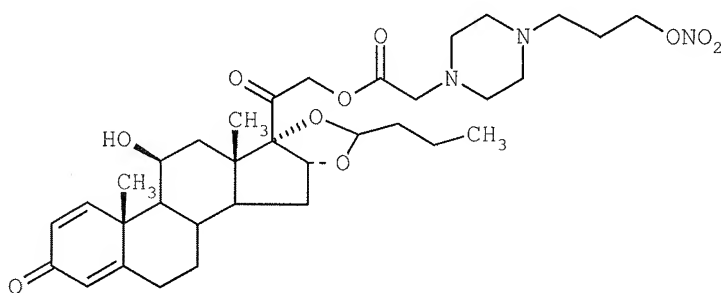
;

Budesonide-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]acetate]



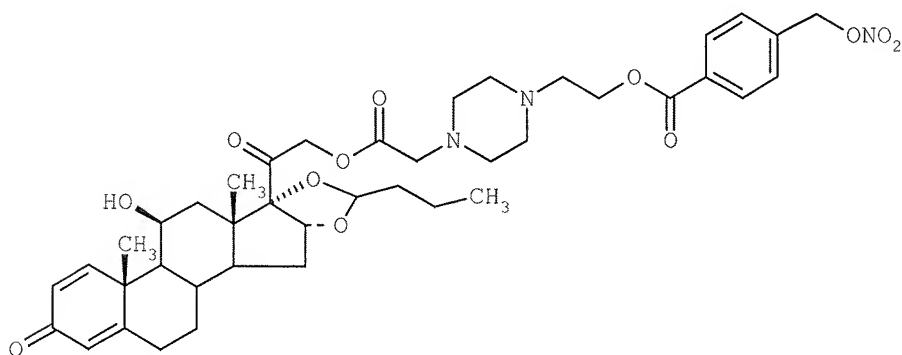
;

Budesonide-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl] acetate]



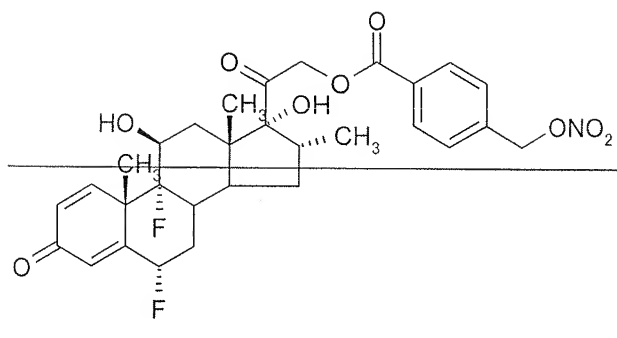
; and

Budesonide-21[2-[4-[2-[4-nitrooxymethyl)benzoyloxy]ethyl]-1-piperazinyl]acetate]

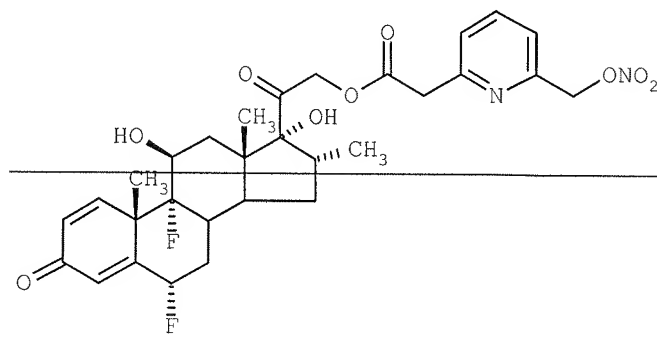


[[;]]

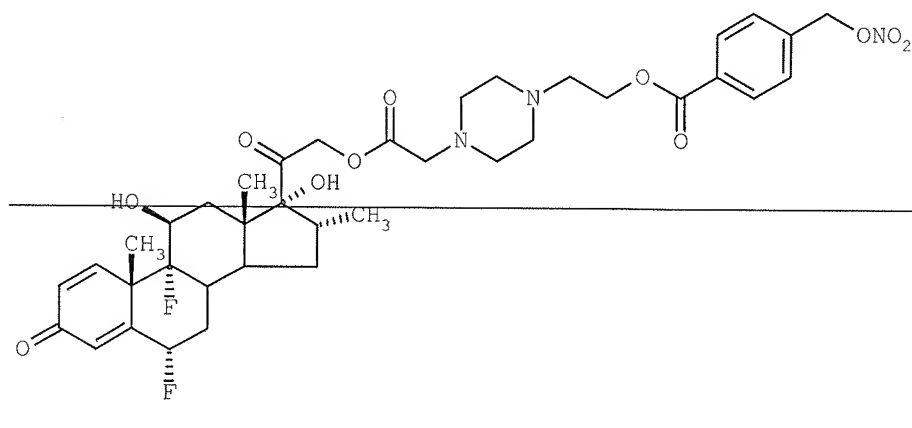
Flumethasone 21-(4'-nitrooxymethyl)benzoate:



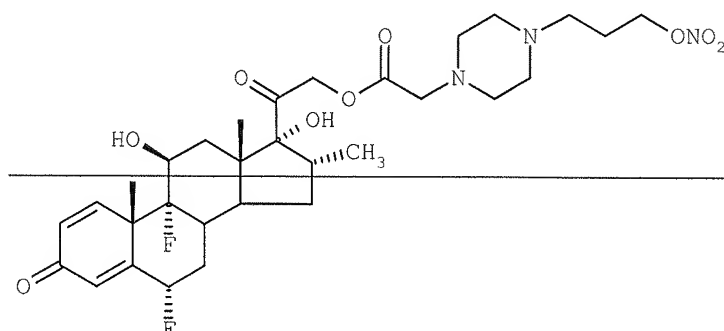
Flumethasone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]acetate]



Flumethasone-21[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy]ethyl]-1-piperazinyl]acetate]

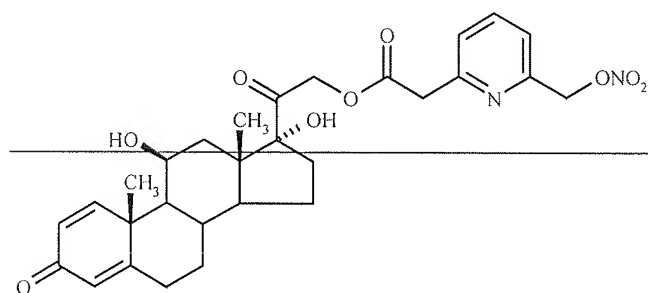


Flumethasone-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl]-acetate]



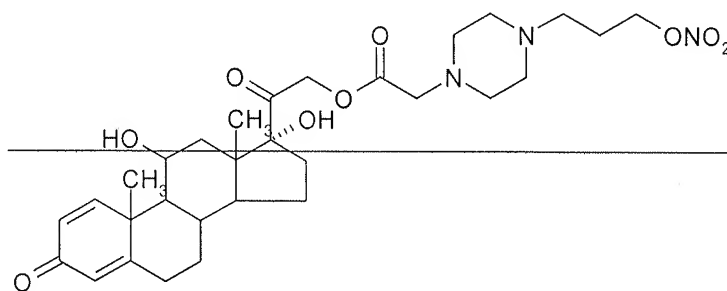
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Prednisolone-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]-acetate]



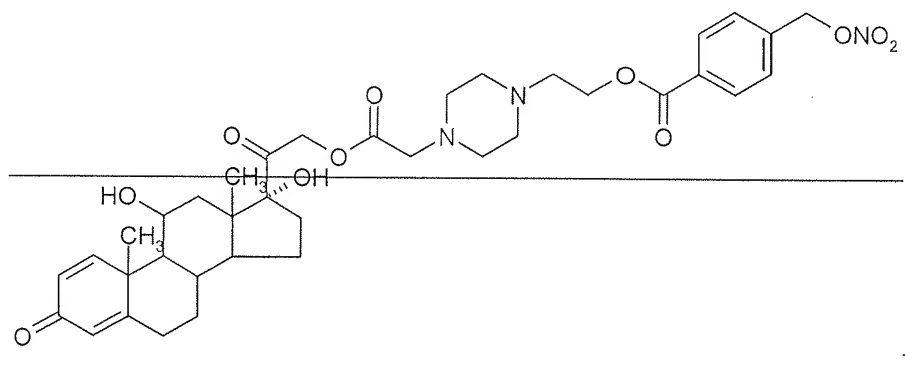
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Prednisolone-21-[2-[4-(3-nitrooxy)propyl] piperazin-1-yl] acetate] and the corresponding bishydrochloride salt:

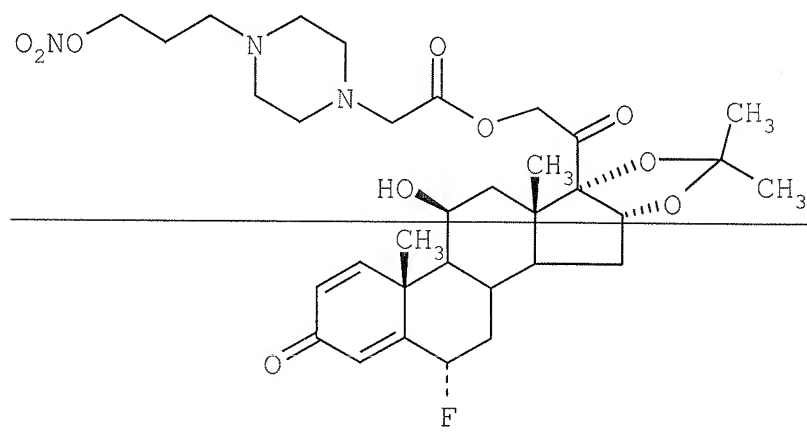


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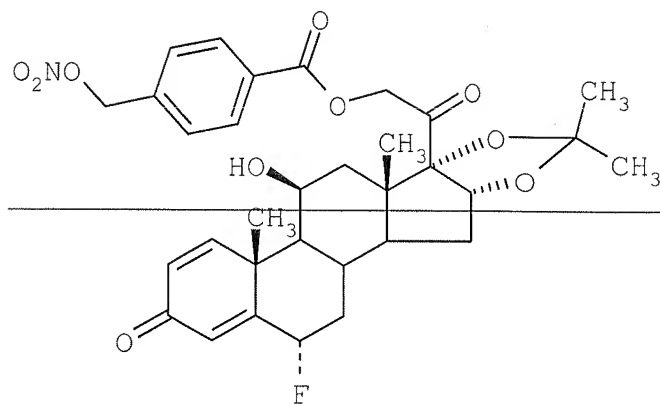
~~Prednisolone-21-[2-[4-[2-[(4'-nitrooxymethyl)benzoyl
oxy]ethyl]piperazin-1-yl]acetate] and the corresponding bishydrochloride salt:~~



~~Flunisolide-21-[2-[4-[3-(nitrooxy)propyl]-1-piperazinyl]-acetate]~~

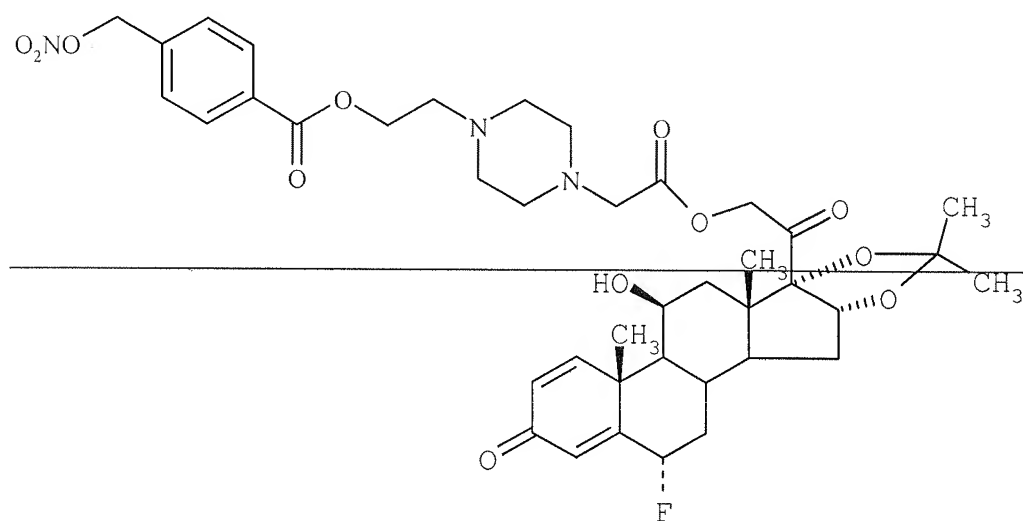


~~Flunisolide-21-[(4'-nitrooxymethyl)]benzoate~~



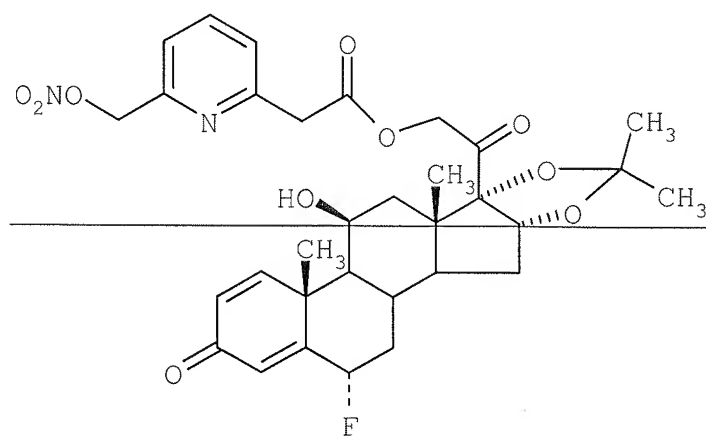
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Flunisolide-21-[2-[4-[2-[4-(nitrooxymethyl)benzoyloxy]ethyl]-1-piperazinyl]acetate]



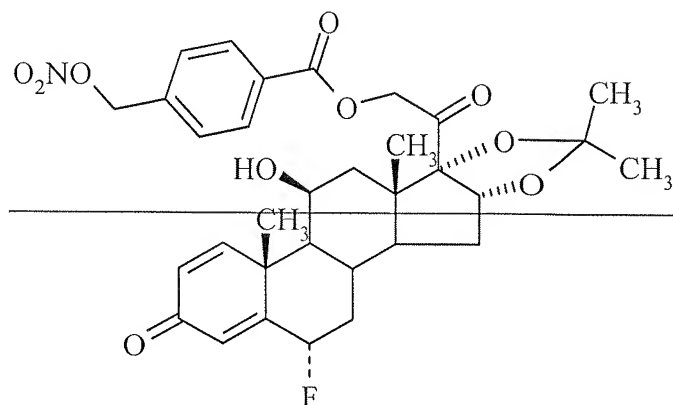
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Flunisolide-21-[2-[6-(nitrooxymethyl)-2-pyridinyl]acetate]



7

Flunisolid 21-[(4'-nitrooxymethyl)benzoate]



Claim 9. (Previously Presented) Use of the compounds according to claim 1, for the preparation of medicaments.

Claim 10. (Previously Presented) Use of the compounds according to claim 1, as drugs having antiinflammatory activity at peripheral level.

Claim 11. (Previously Presented) Use of the compounds according to claim 1, for the therapy of neurodegenerative diseases on an inflammatory and traumatic basis of the nervous system.

Claim 12. (Previously Presented) Use of the compounds according to claim 1, as drugs having an antiarthritic activity.

Claim 13. (Previously Presented) Use of the compounds of claim 1, as drugs having an immunodepressive activity.

Claim 14. (Previously Presented) Use of the compounds according to claim 1, as drugs having an angiostatic/angiogenetic activity.

Claim 15. (Previously Presented) Use of the compounds according to claim 1, as drugs having an antiasthmatic activity.

Claim 16. (Previously Presented) Use of the compounds according to claim 1, in substitutive hormonal therapies, preferably in the post-menopause therapy.

Claim 17. (Previously Presented) Use of the compounds according to claim 1, in rheumatic disease therapies.

Claim 18. (Previously Presented) Use of the compounds according to claim 1, in renal disease therapies.

Claim 19. (Previously Presented) Use of the compounds according to claim 1, in bronchial disease therapies.

Claim 20. (Previously Presented) Use of the compounds according to claim 1, in ocular disease therapies.

Claim 21. (Previously Presented) Use of the compounds according to claim 1, in dermatologic disease therapies.

Claim 22. (Previously Presented) Use of the compounds according to claim 1, in autoimmune disease therapies.

Claim 23. (Previously Presented) Use of the compounds according to claim 1, in tumoral process therapies, optionally in combination with chemotherapeutic and/or radiotherapeutic treatments.

Claim 24. (Original) Use according to claim 10, in inflammatory pathologies affecting the gastrointestinal system.

Claim 25. (Previously Presented) Use of the compounds according to claim 1, wherein the glucocorticoid compounds are used in respiratory pathologies characterized by broncho-obstructive events.

Claim 26. (Currently Amended) ~~Pharmaceutical formulations~~ A pharmaceutical composition comprising the compounds of a compound according to claim 1 and a pharmaceutically acceptable carrier.